



Lipofilling for functional reconstruction of the sole of the foot



Giovanni Nicoletti^{a,b,c,*}, Federica Brenta^{a,b}, Omar Jaber^{a,b}, Enrico Laberinti^d,
Angela Faga^{a,b,c}

^a Plastic and Reconstructive Surgery, Department of Clinical Surgical Diagnostic and Pediatric Sciences, University of Pavia, Via Aselli 45, 27100 Pavia, Italy

^b Plastic and Reconstructive Surgery Unit, Salvatore Maugeri Research and Care Institute, Via Salvatore Maugeri 10, 27100 Pavia, Italy

^c Advanced Technologies for Regenerative Medicine and Inductive Surgery Research Centre, University of Pavia, Viale Brambilla 74, 27100 Pavia, Italy

^d Ortopedia Tecnica di Elio Barbetta, Corso Milano 1, 27029 Vigevano (PV), Italy

ARTICLE INFO

Article history:

Received 23 October 2013

Received in revised form 20 February 2014

Accepted 24 February 2014

Keywords:

Lipofilling

Sole reconstruction

Plantar insole

Rehabilitation

Trauma

ABSTRACT

Background: New advances in regenerative surgery may increase the potential for rehabilitation in the injured foot.

Objectives: A clinical prospective observational study was carried out to assess the effectiveness of lipofilling to improve the functional recovery of the injured foot.

Methods: Four patients with anatomical–functional impairment following repair of post-traumatic soft tissue loss of the foot were involved in the study. All of the patients complained of pain in the repaired plantar weight bearing area, skin instability, recurrent ulcerations and were walking on crutches.

A combined plastic surgery and technical orthopaedic assessment identified the plantar areas requiring anatomical changes for load redistribution. Two selective sequential lipofillings with a 12 weeks' time interval were performed. Manufacturing of custom-made plantar insoles and/or shoes followed each surgical procedure.

Results: After the treatment all of the patients progressively recovered both a better plantar load distribution and a local soft tissue stability, referred the remission of chronic pain and discontinued the use of crutches.

Conclusion: Lipofilling proved to be an effective and versatile surgical technique for both reconstructive and regenerative purposes. The interaction between the Plastic Surgery staff and the Orthopaedic Technician outlined a successful multidisciplinary approach model for the rehabilitation of the injured foot.

© 2014 The Authors. Published by Elsevier Ltd. This is an open access article under the CC BY-NC-SA license (<http://creativecommons.org/licenses/by-nc-sa/3.0/>).

1. Introduction

The reconstruction of the plantar soft tissue of the foot remains a complex and challenging undertaking as it traditionally relies on flaps and skin grafts [1] that often leave disabling after effects. Although flaps provide a stable and effective reconstruction, scars and deformity are often the unavoidable price to pay for such a choice. On the other hand skin graft repair is not a satisfactory therapeutical solution in the injured foot, too. Skin grafts are usually unstable in the long term, are not fit for weight bearing and inexorably undergo retraction with subsequent foot deformity. Pain is the common denominator of all of these after effects.

Orthopaedic Technicians are able to improve the functional performance of a reconstructed foot with custom made plantar insoles and/or shoes. Nevertheless manufacturing of such effective devices is not possible in all of the clinical situations, as in case of severe degree of residual anatomical and functional disruption and deformity.

In our experience the limits of traditional post-reconstructive rehabilitation of the injured foot was overcome by the integration of orthopaedic custom made devices and selective lipofilling.

2. Materials and methods

Four male patients (age 33–71 years) were enrolled in the study over a period of 3 years, from March 2008 to May 2009, at the Plastic and Reconstructive Surgery Unit of the University of Pavia, Salvatore Maugeri Research and Care Institute, Pavia, Italy. All of the patients had undergone repair of post-traumatic soft tissue loss of the foot: three of them with a split thickness skin graft and one with

* Corresponding author at: Plastic and Reconstructive Surgery, University of Pavia, Salvatore Maugeri Research and Care Institute, Via Salvatore Maugeri, 10, 27100 Pavia, Italy. Tel.: +39 0382 592222; fax: +39 0382 592220; mobile: +39 338 5778146.

E-mail addresses: giovanni.nicoletti@unipv.it, giovanni.nicoletti@fsm.it (G. Nicoletti).



Fig. 1. Injection of centrifuged adipose tissue in the recipient site.

a cross-leg fascio-cutaneous flap. They were in good general conditions, had no history of metabolic, chronic skin and/or neurological diseases and did not undergo pharmacological therapies potentially or actually impairing the wound healing process; they also had no history of previous muscular-skeletal disease before injury. All of the patients complained of pain in the repaired plantar weight bearing area, local skin instability with recurrent ulcerations and callus formation and were walking on crutches. At the time of clinical enrolment the patients underwent a combined plastic surgery and technical orthopaedic assessment.

At this stage a podoscopic and podometric study of plantar footprints was carried out using the mirror podoscope and the ink pad system. Each patient was taken dynamic and static plantar footprints in both feet in order to compare the injured foot with the healthy one. The study allowed for screening of both the plantar weight bearing pattern and the sites of potential conflicts with the shoe. The plantar footprint also allowed for identification of the metatarsal heads location, the key for planning the load redistribution. Such procedures allowed to identify the plantar areas requiring the increase of weight bearing surface and tissue thickening. This information was discussed with the surgical staff for outlining of the appropriate operative planning.

Lipofilling was carried out according to modified Coleman's technique [2]. The fat grafts were harvested from the abdominal subcutaneous tissue by using a local superwet saline plus Epinephrine ($1/1 \times 10^{-6}$) infiltration. Syringe liposuction was carried out using 1 mm blunt round tip cannulas [3]. The aspirated fat was processed in a centrifuge at 1500/rpm for 2 min [4] to get the appropriate purified adipose fraction. A gentle meticulous lysis of the scar tissue in the recipient sites was carried out with the blunt round tip cannulas through multiple punctiform skin incisions in order to create multiple subcutaneous tunnels crossing each other in multiple planes. The purified adipose fraction was injected in small amounts in a retrograde direction along these multiple subcutaneous tunnels (Fig. 1).

The patients were advised to avoid both dynamic and static plantar weight bearing in the operated foot for 2 weeks after surgery. A 30% partial dynamic and static plantar weight bearing using crutches and a soft sock was then allowed for the following 2 weeks. At the end of this time, 4 weeks after the surgical procedure, a technical orthopaedic post-operative assessment was scheduled for manufacturing of the custom-made plantar insoles and/or shoes. A progressive recovery of full dynamic and static plantar weight bearing was then allowed within 2 weeks after manufacturing of the custom made plantar insoles and/or shoes.

Adequate fitting of the custom-made devices was checked 4 weeks after full dynamic and static plantar weight bearing recovery



Fig. 2. Case 1. Unstable ulceration on the site of a previous split thickness skin graft on the outer side of the right heel.

and requirements for a further lipofilling were discussed with the surgical staff.

Twelve weeks after the first surgical procedure a second lipofilling session was then carried out. The post-operative static and dynamic plantar weight bearing protocol and the technical orthopaedic procedures repeated the sequence of the first stage.

Eventually the long term follow-up was scheduled yearly once.

In our experience two lipofilling procedures could provide an objective and subjective satisfactory result in all of the cases.

All of the patients signed informed consent forms for both the surgical procedure and the medical photography.

The study was carried out according to the declaration of Helsinki and was approved by the Plastic and Reconstructive Surgery Unit of the University of Pavia, Salvatore Maugeri Research and Care Institute, Pavia, Italy ethical committee.

2.1. Cases report

2.1.1. Case 1

A 33-year-old male patient presented with a 20 mm × 10 mm unstable ulceration on the site of a previous split thickness skin graft on the outer side of the right heel.

The patient referred a domestic accident occurred 15 years before with post-traumatic soft tissue loss of the anterior two thirds of the right heel that was repaired with a split thickness skin graft.

A thick hyperkeratosis was appreciated along the margins of the previously grafted area that appeared atrophic, stiff and retracted. A relevant callus formation was also appreciated in the plantar skin at the level of the metatarsal heads together with a localized malleolar oedema (Fig. 2). The patient was walking on crutches because of the local pain and therefore was forced to a sedentary lifestyle since the time of injury.

The patient underwent lipofilling of the unstable skin grafted area with 30 ml of purified adipose fraction harvested from the lower abdominal subcutaneous region. After manufacturing of a custom made shoe at the end of the post-operative rehabilitation protocol the patient progressively discontinued the use of the crutches due to significant reduction of the local pain. Ten weeks post-operatively the skin graft appeared pliable, stable and trophic. Nevertheless in the grafted heel a relevant surface depression was still appreciated. Therefore a second lipofilling session was carried out 12 weeks after the first one with injection of 25 ml of purified adipose fraction harvested from the lower abdominal subcutaneous region. Following the second surgical stage, the previously



Fig. 3. Case 1. Post-operative appearance after two lipofilling sessions: the improved heel contour and trophism of the grafted skin are appreciated.

manufactured custom made shoe was modified according to the new static and dynamic postural requirements. The superficial soft tissue depression was completely filled with improved trophism and elasticity of the grafted skin. The patient definitely discontinued the use of crutches and referred the complete remission of the local pain. At 3 years' follow-up the result is stable (Fig. 3).

2.1.2. Case 2

A 40-year-old male patient was admitted in our Unit for an acute post-traumatic soft tissue loss of the left foot for a road traffic accident. The soft tissue loss involved the whole heel and the plantar arch (Fig. 4). The patient underwent a thorough debridement and repair with a mesh split thickness skin graft (Fig. 5).

Two years after the skin graft procedure, the foot was still unfit for deambulation due to severe local pain and lack of stable native weight bearing plantar soft tissues at the level of the heel. Rear-foot instability was associated with a marked hyperkeratosis on the plantar skin at the level of the metatarsal heads and of the lateral margin of the sole.

The patient underwent lipofilling of the skin grafted area with 50 ml of purified adipose fraction harvested from the lower abdominal subcutaneous region.

After manufacturing of a custom made shoe at the end of the post-operative rehabilitation protocol the patient progressively recovered deambulation with the aid of crutches and referred a



Fig. 5. Case 2. Soft tissue repair with meshed split thickness skin graft showing close adhesion of the graft to the bone.

significant reduction of the local pain. Ten weeks post-operatively the skin graft appeared pliable, stable and trophic. Nevertheless in the skin grafted areas a relevant surface depression was still appreciated. Therefore a second lipofilling session was carried out 12 weeks after the first one with injection of 25 ml of purified adipose fraction harvested from the lower abdominal subcutaneous region. Injection involved the skin grafted areas and the subcutaneous tissue in the native plantar skin at the level of the metatarsal heads, too. Following the second surgical stage, the previously manufactured custom made shoe was modified according to the new static and dynamic postural requirements. The superficial soft tissue depression was completely filled with improved trophism and elasticity of the grafted skin. The patient definitely discontinued the use of crutches and referred the complete remission of the local pain. At 3 years' follow-up the result is stable (Fig. 6).

2.1.3. Case 3

A 40-year-old male patient presented with a 15 mm × 10 mm unstable ulceration on the site of a previous split thickness skin graft on the outer side of the left heel associated with severe left foot equinus and rearfoot instability preventing deambulation (Fig. 7).

The patient referred a road traffic accident occurred 2 years before with post-traumatic soft tissue loss of the outer side of the left heel that was repaired with a split thickness skin graft. The patient referred pain in foot pronation and supination. Oedema in



Fig. 4. Case 2. Severe post-traumatic soft tissue loss of the left foot involving the whole heel and the plantar arch.



Fig. 6. Case 2. Post-operative appearance after two lipofilling sessions: the improved foot contour and calcaneal soft tissue padding are appreciated.



Fig. 7. Case 3. Unstable ulceration on the site of a previous split thickness skin graft on the outer side of the left heel.

the foot and in the leg was associated with a marked hyperkeratosis on the plantar skin at the level of the metatarsal heads and of the remaining area of native plantar skin in the heel.

The patient underwent lipofilling of the skin grafted area and of the dorsum of the foot with 50 ml of purified adipose fraction harvested from the lower abdominal subcutaneous region.

A custom made shoe was manufactured at the end of the post-operative rehabilitation protocol and the patient progressively recovered deambulation with the aid of crutches and referred a significant reduction of both the local pain and oedema.

Ten weeks post-operatively the plantar ulceration healed and the skin graft appeared pliable, stable and trophic.

A second lipofilling session was carried out 12 weeks after the first one with injection of 36 ml of purified adipose fraction harvested from the lower abdominal subcutaneous region. Injection involved the skin grafted area and the dorsum of the foot.

Following the second surgical stage, the previously manufactured custom made shoe was modified according to the new static and dynamic postural requirements.

The superficial soft tissue depression was completely filled with improved trophism and elasticity of the grafted skin. Furthermore equinus and local oedema cleared up and rearfoot stability significantly improved.

The patient definitely discontinued the use of crutches and referred the complete remission of the local pain. At 3 years' follow-up the result is stable (Fig. 8).



Fig. 8. Case 3. Post-operative appearance after two lipofilling sessions: the improved heel contour and trophism of the grafted skin are appreciated.



Fig. 9. Case 4. Unstable ulceration on the left heel at the junction between the native plantar skin and a previous cross-leg fascio-cutaneous flap.

2.1.4. Case 4

A 71-year-old male patient presented with a 20 mm × 20 mm unstable ulceration on the left heel at the junction between the native plantar skin and a previous cross-leg fascio-cutaneous flap that prevented weight bearing and deambulation (Fig. 9).

The patient referred an accident at work occurred 25 years before with post-traumatic soft tissue loss of the whole left heel that was repaired with a cross-leg fascio-cutaneous flap.

The patient underwent thorough debridement of the ulcer and repair with a local transposition flap harvested within the previous cross-leg fascio-cutaneous flap (Fig. 10).

Following such a repair several depressions and irregularities were appreciated in the reconstructed heel and prevented an adequate static and dynamic plantar weight bearing.

The patient underwent lipofilling of the left heel with 36 ml of purified adipose fraction harvested from the lower abdominal subcutaneous region.

The patient was then advised to keep avoiding both dynamic and static plantar weight bearing in the operated foot for further 2 weeks after the lipofilling procedure. A partial dynamic and static plantar weight bearing was then allowed for the following 2 weeks.

A custom made shoe was manufactured at the end of this post-operative rehabilitation protocol and the patient progressively recovered deambulation with the aid of crutches.

A second lipofilling session was carried out 12 weeks after the first one with injection of 28 ml of purified adipose fraction



Fig. 10. Case 4. Debridement of the ulcer and repair with a local transposition flap harvested within the previous cross-leg fascio-cutaneous flap. Depressions and irregularities are still appreciated in the reconstructed heel contour.



Fig. 11. Case 4. Post-operative appearance after two lipofilling sessions: the improved overall heel contour is appreciated.

harvested from the lower abdominal subcutaneous region. Injection provided filling of some remaining depressed areas in the left heel.

Following the second surgical stage, the previously manufactured custom made shoe was modified according to the new static and dynamic postural requirements. Furthermore, a custom made plantar insole was manufactured for fitting in a sport shoe thus allowing the patient to go back to cycling.

Lipofilling significantly reduced the soft tissue depressions and irregularities in the left heel and allowed recovery of both static and dynamic plantar weight bearing.

At 3 years' follow-up the result is stable (Fig. 11).

3. Discussion

Lipofilling is a particular technique of fat grafting, that has gained an increased popularity in the last 20 years for both cosmetic and reconstructive purposes.

Since Zuk in 2002 demonstrated that human adipose tissue is a source of multipotent stem cells, literature has increased exponentially on the characterization of fat derived cells and on the clinical use of fat transfer for regenerative applications [5].

It is widely accepted that mature adipose cells act as biological niche for mesenchymal stem cells with multi-potent differentiation potential, the so called Adipose Derived Stem Cells (ADSC) [5]. Nevertheless the actual fate and effects of the grafted adipose tissue after the process of transfer is still under study. The exact fate and effects of the grafted fat are supposed to be influenced by the variable contribution of different factors: a part of the native adipose cells from the donor site survive the process of transfer; new adipose cells might derive from the development and growth of pre-adipocytes from the graft; multipotent stem cells from the graft might develop and grow along many different cellular lines; the paracrine release of growth factors by the Adipose Derived Stem Cells (ADSC) from the graft can stimulate the development and growth of many different cellular lines in the recipient site [6–8].

The effectiveness of lipofilling in the treatment of scars has been widely recognized over the last 5 years [9]. Lipofilling may therefore provide a regenerative boost in the recipient tissues with enhancement of the local wound repair and tissue regeneration processes [10–12].

In our experience, the use of lipofilling for the treatment of disabling after effects following reconstruction of the sole allowed for a significant improvement of the functional–anatomical status of the injured foot. The key for success was the close cooperation between the Plastic Surgery staff and the Orthopaedic Technician as the latter could manufacture custom made plantar insoles

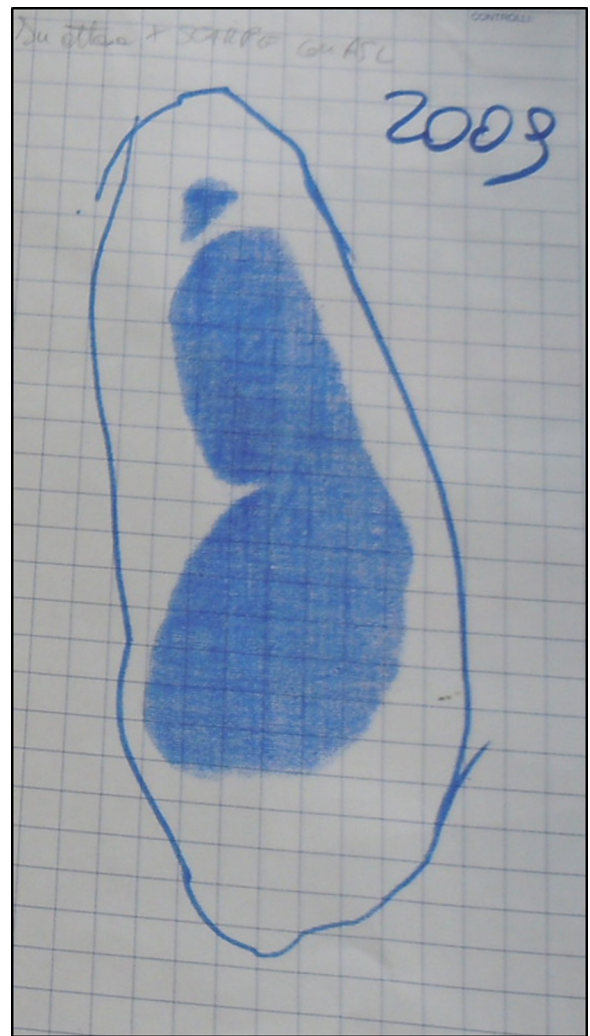


Fig. 12. Left footprint before treatment.

and/or shoes that allowed the patients the best possible physiological deambulation [13,14]. The accurate static and dynamic podometric study could identify the actual plantar weight bearing pattern in the injured foot. Comparison with the contralateral healthy foot allowed for an accurate selective lipofilling planning aiming to improve the weight bearing pattern with eventual better load distribution (Figs. 12–14).

Our study involved a quite homogeneous sample of patients featuring a similar clinical picture with chronic stabilized post-traumatic signs and symptoms: recurrent ulcerations, callus formation, dry skin, rear-foot unbalance, metatarsal heads overload, malleolar oedema and pain.

Lipofilling is a fat transfer without its native blood supply whose survival relies on the recipient site vascular network. It is well known that any graft takes according to a standard sequence of local biological events pivoted by the growth of a new vascular network from the recipient site to the graft. Post-operative immobilization of a grafted site is the key to allow the establishment of these new mutual vascular connections. In our experience we applied to the lipofilling procedure the same post-operative local immobilization protocol routinely in use for skin grafts in the leg and foot. For this reason we advised the patient to abstain from static and dynamic plantar weight bearing for the first 2 weeks after surgery, to apply 30% partial load in the following 2 weeks and to expect a full static and dynamic plantar weight bearing at 6 weeks after surgery.



Fig. 13. Left footprint 1 year post-operatively.

The exact rate of take of an adipose graft is controversial in the literature [15–21] and although a recent prospective long term multicenter study demonstrated with objective measurements a $55 \pm 18\%$ grafted fat survival [22] the ability to judge the overall success of fat grafting remains limited [23]. Gentle surgical handling and centrifugation is the key for obtaining higher rates of graft take [2–4].

Lipofilling proved to be a safe procedure in an increasing number of clinical indications except in actual or potential tumour beds where the “tumour–stroma interaction” can potentially induce cancer reappearance by “fueling” dormant cancer cells [24]. Higher risk of development of breast intraepithelial neoplasia patients and late local recurrence of osteosarcoma after lipofilling have been reported [25,26].

The current consensus is that the volume of injected fat might be considered substantially stable at 50 days [27]. Therefore our treatment with sequential lipofilling was scheduled at 12 weeks’ time interval and discontinued when a satisfactory stable clinical result was achieved. Two sequential lipofillings sufficed to get such a goal in all of our cases.

The assessment of the outcomes was carried out with a clinical observation by both the surgeon and the orthopaedic technician focusing on new shape stability, ulceration remission, hyperkeratosis and oedema reduction, local tissue trophism improvement,

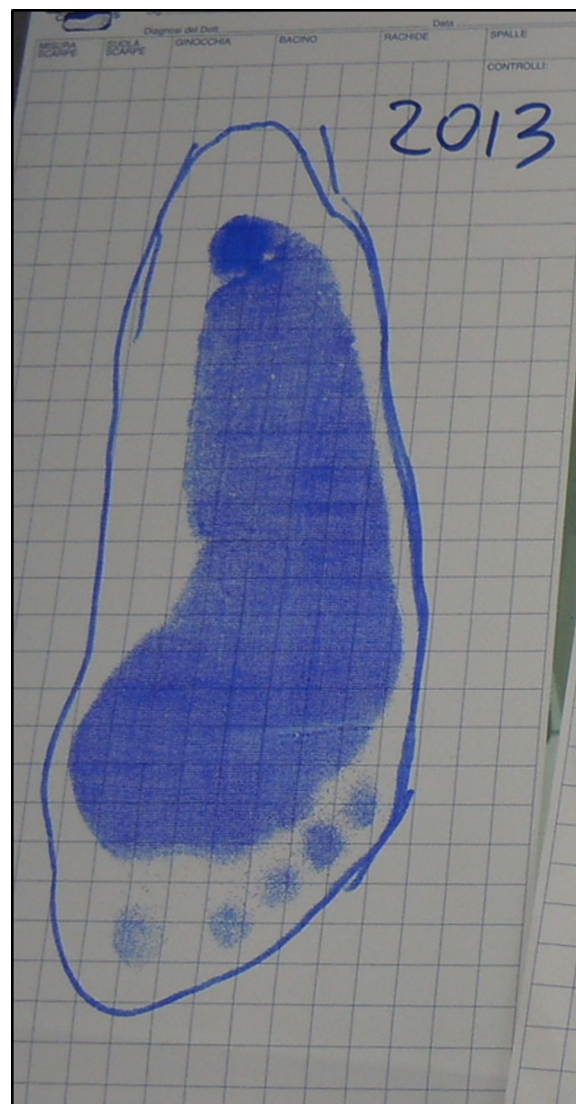


Fig. 14. Left footprint 4 years post-operatively: weight bearing redistribution with functional rehabilitation allowed eventual recruitment of the toes in the gait.

plantar load redistribution, pain reduction and deambulation recovery.

Lipofilling allowed for achievement of the following objectives:

- Increase of the weight bearing surface of the sole with subsequent rear-foot re-balance. The improved plantar load redistribution allowed for an improved gait pattern with less traumatic deambulation and subsequent reduction in callus formation and ulceration recurrence. Furthermore such an improvement allowed for an increase in the lower limb muscular pump with a subsequent more efficient lymphatic drainage and eventual chronic oedema reduction.
- Significant improvement of local tissue trophism with subtotal pain remission.
- Manufacturing of a more effective custom made orthopaedic device.

All of these results allowed for a progressive and complete recovery of unassisted deambulation and postural balance stabilization.

The main goal of our study was the assessment of the clinical benefits in a small group of patients with chronic stabilized

post-traumatic severe degree of functional impairment of the foot. Therefore our report might be considered an evidence based medicine experience.

4. Conclusions

Lipofilling proved to be an extremely effective and versatile surgical technique for both reconstructive and regenerative purposes in the injured foot. Our experience of close interaction between the Plastic Surgery staff and the Orthopaedic Technician outlined a successful multidisciplinary approach model for the post-traumatic rehabilitation of the foot.

Acknowledgements

The authors have not any commercial associations or financial disclosures that might pose or create a conflict of interest with information presented in this manuscript.

The authors wish to thank Floriana Cazzola for her much appreciated technical support.

References

- [1] Sommerlad BC, McGrouther DA. Resurfacing the sole: long-term follow-up and comparison of techniques. *British Journal of Plastic Surgery* 1978;31(2):107–16.
- [2] Coleman SR. Facial recontouring with lipofstructure. *Clinics in Plastic Surgery* 1997;24(2):347–67.
- [3] Ozsoy Z, Kul Z, Bilir A. The role of cannula diameter in improved adipocyte viability: a quantitative analysis. *Aesthetic Surgery Journal* 2006;26(3):287–9.
- [4] Kurita M, Matsumoto D, Shigeura T, Sato K, Gonda K, Harii K, et al. Influences of centrifugation on cells and tissues in liposuction aspirates: optimized centrifugation for lipotransfer and cell isolation. *Plastic and Reconstructive Surgery* 2008;121(3):1033–41.
- [5] Zuk PA, Zhu M, Ashjian P, De Ugarte DA, Huang JL, Mizuno H, et al. Human adipose tissue is a source of multipotent stem cells. *Molecular Biology of the Cell* 2002;13(12):4279–95.
- [6] Dong Z, Peng Z, Chang Q, Lu F. The survival condition and immunoregulatory function of adipose stromal vascular fraction (SVF) in the early stage of nonvascularized adipose transplantation. *PLOS ONE* 2013;8(November (11)):e80364.
- [7] Torio-Padron N, Huotari AM, Eisenhardt SU, Borges J, Stark GB. Comparison of pre-adipocyte yield, growth and differentiation characteristics from excised versus aspirated adipose tissue. *Cells, Tissues, Organs* 2010;191:365–71.
- [8] Eto H, Kato H, Suga H, Aoi N, Doi K, et al. The fate of adipocytes after nonvascularized fat grafting: evidence of early death and replacement of adipocytes. *Plastic and Reconstructive Surgery* 2012;129(5):1081–92.
- [9] Klinger M, Marazzi M, Vigo D, Torre M. Fat injection for cases of severe burn outcomes: a new perspective of scar remodeling and reduction. *Aesthetic Plastic Surgery* 2008;32(3):465–9.
- [10] Zuk PA. The adipose-derived stem cell: looking back and looking ahead. *Molecular Biology of the Cell* 2010;21(1):1783–7.
- [11] Schaffler A, Buchler C. Concise review: adipose tissue-derived stromal cells – basic and clinical implications for novel cell-based therapies. *Stem Cells* 2007;25(4):818–27.
- [12] Nakagami H, Morishita R, Maeda K, Kikuchi Y, Ogihara T, Kaneda Y. Adipose tissue-derived stromal cells as a novel option for regenerative cell therapy. *Journal of Atherosclerosis and Thrombosis* 2006;13(2):77–81.
- [13] Roberts ME, Gordon CE. Orthopedic footwear. Custom-made and commercially manufactured footwear. *Foot and Ankle Clinics* 2001;6(2):243–7.
- [14] van Netten JJ, Jannink MJ, Hijmans JM, Geertzen JH, Postema KJ. Use and usability of custom-made orthopedic shoes. *Journal of Rehabilitation Research and Development* 2010;47(1):73–81.
- [15] Rubino C, Mazzarello V, Faenza M, Montella A, Santanelli F, Farace F. A scanning electron microscope study and statistical analysis of adipocyte morphology in lipofilling: comparing the effects of harvesting and purification procedures with 2 different techniques. *Annals of Plastic Surgery* 2013;(October). PubMed PMID: 24149403 [Epub ahead of print].
- [16] Køllef SF, Fischer-Nielsen A, Mathiasen AB, Elberg JJ, Oliveri RS, Glovinski PV, et al. Enrichment of autologous fat grafts with ex-vivo expanded adipose tissue-derived stem cells for graft survival: a randomised placebo-controlled trial. *Lancet* 2013;382(9898):1113–20.
- [17] Peltoniemi HH, Salmi A, Miettinen S, Mannerström B, Saariniemi K, Mikkonen R, et al. Stem cell enrichment does not warrant a higher graft survival in lipofilling of the breast: a prospective comparative study. *Journal of Plastic, Reconstructive & Aesthetic Surgery* 2013;66(11):1494–503.
- [18] Karagianni M, Kraneburg U, Klüter H, Machens HG, Bieback K, Schantz JT, et al. Autologous fat grafts and supportive enrichment with adipose tissue stromal cells. *Handchirurgie, Mikrochirurgie, Plastische Chirurgie* 2013;45(2):93–8.
- [19] Agostini T, Lazzeri D, Pini A, Marino G, Li Quattrini A, Bani D, et al. Wet and dry techniques for structural fat graft harvesting: histomorphometric and cell viability assessments of lipoaspirated samples. *Plastic and Reconstructive Surgery* 2012;130(2):331e–9e.
- [20] Trojahn Køllef SF, Oliveri RS, Glovinski PV, Elberg JJ, Fischer-Nielsen A, Drzewiecki KT. Importance of mesenchymal stem cells in autologous fat grafting: a systematic review of existing studies. *Journal of Plastic Surgery and Hand Surgery* 2012;46(2):59–68.
- [21] Khater R, Atanassova P, Anastassov Y, Pellerin P, Martinot-Duquennoy V. Clinical and experimental study of autologous fat grafting after processing by centrifugation and serum lavage. *Aesthetic Plastic Surgery* 2009;33(1):37–43.
- [22] Khouri RK, Eisenmann-Klein M, Cardoso E, Cooley BC, Kacher D, Gombos E, et al. Brava and autologous fat transfer is a safe and effective breast augmentation alternative: results of a 6-year, 81-patient, prospective multicenter study. *Plastic and Reconstructive Surgery* 2012;129(May (5)):1173–87.
- [23] Choi M, Small K, Levovitz C, Lee C, Fadl A, Karp NS. The volumetric analysis of fat graft survival in breast reconstruction. *Plastic and Reconstructive Surgery* 2013;131(2):185–91.
- [24] Lohsiriwat V, Curigliano G, Rietjens M, Goldhirsch A, Petit JY. Autologous fat transplantation in patients with breast cancer: silencing or fueling cancer recurrence? *Breast* 2011;20(August (4)):351–7.
- [25] Petit JY, Rietjens M, Botteri E, Rotmensz N, Bertolini F, Curigliano G, et al. Evaluation of fat grafting safety in patients with intraepithelial neoplasia: a matched-cohort study. *Annals of Oncology* 2013;24(June (6)):1479–84.
- [26] Perrot P, Rousseau J, Bouffaut AL, Rédini F, Cassagnau E, Deschaseaux F, et al. Safety concern between autologous fat graft, mesenchymal stem cell and osteosarcoma recurrence. *PLoS ONE* 2010;5(June (6)):e10999.
- [27] Rigotti G. Discussion the volumetric analysis of fat graft survival in breast reconstruction. *Plastic and Reconstructive Surgery* 2013;131(2):192–3.